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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/634,869	08/06/2003	Gary Michael Kayajanian		7616

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EXAMINER	
ANDERSON, JAMES D	
ART UNIT	PAPER NUMBER
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/24/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/634,869	KAYAJANIAN, GARY MICHAEL	
	Examiner	Art Unit	
	James D. Anderson	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2 sheets*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed 7/17/2006 and 7/31/2006, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Status of the Claims

Claims 1-20 are currently pending and are the subject of this Office Action. Claim 20 is withdrawn from consideration as being drawn to non-elected subject matter. Claims 1-19 are presently under examination.

Specification

The abstract of the disclosure is again objected to because it does not describe the claimed invention. Correction is required. See MPEP § 608.01(b).

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 7/17/2006 was considered by the examiner to the extent that each reference cited therein is a proper citation. Please note that the Kayajanian manuscript (2003) was not considered because it is not a published document. Also, citation of Applicant's arguments, etc. on the IDS is not appropriate. These citations have been lined through.

Claim Rejections - 35 USC § 112 (1st Paragraph)

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12 are again rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a Written Description rejection.

The instant claims recite the limitation "arsenic level" but it is not clear how the level of arsenic will be increased and/or maintained and what form of arsenic will be used (*e.g.* As_2O_3, As_4O_6, etc.) to increase the arsenic level in drinking water. In addition, Applicant has not indicated if this method will be used to increase the level of arsenic in drinking water worldwide or in a limited area. For example, the limitation "drinking water" could be interpreted as an 8 oz. glass of water. It is not clear how one would practice the claimed invention since no guidance is provided in how one would increase the level of arsenic in an 8 oz. glass of water (form of arsenic, amount of arsenic, etc.) and whether simply drinking an 8 oz. glass of water having 25 to 75 μg/L arsenic will result in the claimed effect of reducing total cancer morbidity and mortality.

Claims 1-19 are again rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains,

or with which it is most nearly connected, to make and/or use the invention. This is an Enablement Rejection.

In the instant case, Applicant provides no evidence, aside from citing and interpreting three data sets, that increasing levels of arsenic in drinking water will lead to decreased cancer and heart disease mortalities. In fact, as Applicant has noted, EPA regulators and scientists have shown that arsenic is carcinogenic at multiple tissue sites. In addition, the EPA recently set forth a new regulation of a maximum of 10 μg/L total arsenic in drinking water, thereby lowering the previous maximum from 50 to 10 ppb. The EPA estimates that reducing arsenic from 50 to 10 μg/L will prevent ~19-31 cases of bladder cancer and ~5-8 deaths due to bladder cancer per year. The EPA further estimates that reducing arsenic from 50 to 10 μg/L will prevent ~19-25 cases of lung cancer and ~16-22 deaths due to lung cancer per year (*Technical Fact Sheet: Final Rule for Arsenic in Drinking Water*, published January 2001, accessed from www.epa.gov on April 17, 2006).

Further, studies have linked long-term exposure to arsenic in drinking water to cancer of the bladder, lungs, skin, kidney, nasal passages, liver, and prostate. Non-cancer effects of ingesting arsenic include cardiovascular, pulmonary, immunological, neurological, and endocrine (*e.g.*, diabetes) effects. Short-term exposure to high doses of arsenic can cause other adverse health effects, but such effects were unlikely to occur from U.S. public water supplies that were in compliance with the previous arsenic standard of 50 ppb. EPA set the previous standard of 50 ppb in 1975, based on a Public Health Service standard originally established in 1942. A March 1999 report by the National Academy of Sciences concluded that the current

standard does not achieve EPA's goal of protecting public health and should be lowered as soon as possible.

The following is taken directly from the *EPA Fact Sheet on Arsenic in Drinking Water* (published January 2001, accessed from www.epa.gov on April 17, 2006):

> On June 22, 2000, EPA proposed a new drinking water standard of 5 ppb for arsenic and requested comment on options of 3 ppb, 10 ppb and 20 ppb. EPA evaluated over 6,500 pages of comments from 1,100 commenters. EPA set the new arsenic standard for drinking water at 10 ppb to protect consumers against the effects of long-term, chronic exposure to arsenic in drinking water. EPA used its discretionary authority under the 1996 Amendments to the Safe Drinking Water Act to set the standard at a level that "maximizes health risk reduction benefits at a cost that is justified by the benefits." The new standard will apply to all 54,000 community water systems. A community water system is a system that serves 15 locations or 25 residents year-round, including most cities and towns, apartments, and mobile home parks with their own water supplies. EPA estimates that roughly five percent, or 3,000, of community water systems, serving 11 million people, will have to take corrective action to lower the current levels of arsenic in their drinking water. The new standard also applies to 20,000 water systems that serve at least 25 of the same people more than six months of the year, such as schools, churches, nursing homes, and factories. EPA estimates that five percent, or 1,100, of these water systems, serving approximately 2 million people, will need to take measures to meet the new arsenic standard. Of all of the affected systems, 97 percent are small systems that serve fewer than 10,000 people each.

Given the above regulation which set an upper limit of 10 μg/L total arsenic in drinking water and the profound evidence that arsenic is linked to numerous cancers and other health problems, the present invention is not enabled for claims to reduce cancer and heart disease related deaths by increasing the arsenic in drinking water to between 2.5 and 7.5x the current standard. This is especially true given that the previous standard of 50 μg/L was reduced to the current level of 10 μg/L because of the increased risk of cancer and other health problems.

Thus, undue experimentation would be required in order to practice the claimed invention of reducing cancer and heart disease related deaths by increasing the level of arsenic in drinking water.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The Court in *Wands* states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicted on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*id.*). The factors to be considered in determining whether undue experimentation is required include:

(1) the quantity of experimentation necessary,

(2) the amount or direction or guidance presented,

(3) the presence or absence of working examples,

(4) the nature of the invention,

(5) the state of the prior art,

(6) the relative skill of those in the art,

(7) the predictability or unpredictability or the art, and

(8) the breadth of the claims.

While all of these factors are considered, a sufficient amount of *prima facie* case is discussed below.

The instant specification fails to provide guidance that would allow the skilled artisan to practice the instant invention without resorting to undue experimentation, as discussed in the subsections set forth below:

1. The quantity of experimentation necessary

The skilled artisan would expect a method of reducing cancer and heart disease morbidity and mortality to be the result of the interactions of multiple biological pathways and therefore, highly unpredictable, absent a clear understanding of the structural and biochemical basis for the absolute reduction in cancer and heart disease morbidity and mortality. The instant specification sets forth no such understanding or any criteria for extrapolating beyond those methods actually demonstrated.

The burden of enabling the prevention or reduction of cancer and heart disease mortality (*i.e.* the need for additional testing) would be greater than that of enabling a *treatment* of a specific cancer or form of heart disease. In the instant case, the specification does not provide guidance as to how one skilled in the art would go about reducing cancer and heart disease mortality or how a human could be prevented from developing cancer or heart disease by simply increasing the level of arsenic in drinking water. Further, there is no guidance provided as to a specific protocol to be utilized in order to prove the efficacy of the presently claimed method of reducing cancer or heart disease mortality in a human. Specifically, it is highly unlikely, and the Office would require experimental evidence to claims such as those of instant claims 1-19, which

claim to reduce total cancer mortality in men and women by increasing the level of arsenic in drinking water, for example.

2. The amount of direction or guidance provided

The specification provides no direction for ascertaining how to absolutely reduce total cancer and heart disease morbidity and mortality and the Applicant has not demonstrated that the method of increasing the level of arsenic in drinking water, for example, can reasonably be expected, *a priori*, to exhibit the requisite reduction in total cancer or heart disease mobidity and mortality. Further, Applicant has provided no guidance or direction on how increasing the level of arsenic in drinking could be used to absolutely reduce total cancer or heart disease mobidity and mortality. Applicant argues, "common sense allows for arsenic to be added to drinking water, under conditions described in the invention". This is not persuasive. Applicant has not provided any specific guidance on what type of arsenic is to be added, what drinking water is being treated with arsenic, or how one skilled in the art will actually monitor and verify the effect of increasing the level of arsenic in drinking water. In fact, all Applicant has done is reinterpret epidemiological data sets and arrived at a different conclusion than previous scientists and skilled artisans.

Further, the claims are directed to methods for reducing cancer morbidity and mortality in men and women by "**adjusting** the arsenic level in drinking water to 25-<75 μg/L". Clearly, "adjusting" means raising or lowering. If the arsenic level is above 75 μg/L, adjusting to 25-<75 μg/L would require that the level of arsenic be lowered. Applicant has again provided no

guidance or direction on any methods of lowering the level of arsenic in drinking water to the instantly claimed levels.

3. Presence or absence of working samples

There are no working examples demonstrating that increasing the level of arsenic in drinking water to between 25 and 75 μg/L will lead to a reduction in total cancer or heart diseases related morbidity and mortality. Only anecdotal evidence in the form of data sets is provided, but their interpretation is subjective and not evidence that the claimed methods will result in a decrease in cancer and/or heart disease related morbidity and mortality. Further, the referenced data sets only compare total cancer related deaths, not cancer deaths from specific types of cancer. Thus, it is not clear from the specification if one particular type of cancer was affected more than the others and led to biased results and interpretation of those results.

4. The nature of the invention

The claimed invention relates to a method of reducing total cancer and heart disease related morbidity and mortality by increasing the level of arsenic in drinking water to a value 2.5 to 7.5x the current EPA standard of 10 μg/L.

5. State of the prior art

Applicant has interpreted three data sets to provide evidence that arsenic levels in drinking water can have an effect on cancer and heart disease related deaths. However, no scientific studies have been carried out to determine the effect of arsenic on cancer and heart

disease related deaths. In fact, the prior art demonstrates that arsenic is a carcinogen at high doses. In addition, arsenic-containing compounds vary in toxicity to mammals according to valence state, form (inorganic or organic), physical state (gas, solution, or powder) and factors such as solubility, particle size, rates of absorption and elimination, and presence of impurities. The claims do not state what form, valence state, physical state, etc. of arsenic will be used in the present method. The prior art is clear that chronic arsenic exposure **causes** various cancers and other health issues. There is no evidence provided in the specification to the contrary, aside from the aforementioned anecdotal evidence and the Applicant's interpretation of three separate data sets.

6. Relative skill of those in the art

The relative skill of those in the art is generally that of a Ph.D. or M.D.

7. Predictability of the art

In the instant case, Claims 1-19 are drawn to methods of reducing total cancer and heart disease related morbidity and mortality by increasing the level of arsenic in drinking water to 2.5 to 7.5x the current EPA standard. The specification provides an interpretation of three epidemiology data sets that the Applicant asserts provides support for the current claims. However, there are no working examples or referenced scientific studies that provide support for the claimed invention. In fact, the prior art teaches away from the current methods. Arsenic is a known carcinogen as is evidenced by references cited by the Applicant. Applicant admits that lower and higher levels of arsenic than those claimed are harmful to humans but provides no

evidence that the instantly claimed levels are safe and will result in the intended result (*i.e.* reduction in cancer and heart disease related deaths). Further, Morales *et al.* (2000) (cited by applicant) state, "[O]ur analysis suggests that the current standard of 50 μg/L [arsenic in drinking water] is associated with a substantial increased risk of cancer and is not sufficiently protective of human health" (Abstract). Thus, it is clear that analysis of identical data sets is subjective. The fact that applicant has a different interpretation of the data is not sufficient to enable the instantly claimed invention.

As such, the anecdotal evidence of the data sets cannot provide adequate support for the claimed invention since only arsenic levels and cancer mortality were compared. There is no evidence in the data sets that arsenic exposure was directly related to a decrease in cancer death. Further, Applicant only compared total cancer deaths to arsenic levels. However, the claimed method is drawn to different types of cancers. If one type of cancer death was reduced more than others this would lead to a biased interpretation of the data sets. The nature of the invention is complex, being directed to biological and physiological processes and the manipulation of those processes to reduce cancer and heart disease mortality in humans by increasing the level of arsenic in drinking water. The state of the prior art is silent with respect to whether or not arsenic is effective in eliciting the claimed result. In fact, it is clear from the prior art that chronic exposure to arsenic causes cancer and other health problems. Further, the EPA recently lowered the maximum containment level of arsenic in drinking water from 50 to 10 ppb.

Whether or not a particular biological molecule will have an effect in reducing cancer or heart disease mortality in humans is unpredictable, in that it requires empirical screening over a long period of time. In view of all of these factors and the lack of description in the disclosure

regarding the use of the present compounds in eliciting a reduction in total cancer or heart disease mortality in humans, undue experimentation would be required of the skilled artisan to practice the claimed invention.

Given the above, it is clear that the art to which the instant invention relates involves a relatively high degree of unpredictability.

8. Breadth of the Claims

The claims are drawn to methods of 1) reducing total cancer morbidity and mortality in men and women (claims 1-11), 2) reducing heart disease mortality in men (claim 12), and 3) a method for not increasing total cancer morbidity and mortality in humans by increasing and maintaining the level of arsenic in drinking water.

In light of the above analysis the specification clearly fails to enable one of ordinary skill in the art to practice and use the methods of Claims 1-19.

Claim Rejections - 35 USC § 112 (2nd Paragraph)

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 and 12-19 are again rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite the limitation "25-<75 μg/L" but the meaning of the arrangement of the symbolic notations is unclear. Applicant argues that

examiner is not interpreting the notation correctly and acknowledges, "[W]ords are preferable to symbols in this phrase". However, applicant has not amended the claims to overcome this rejection.

Response to Arguments

Firstly, Applicant repeatedly uses the word "patent" to describe the present application. Examiner respectfully reminds Applicant that a patent application is being examined, not a patent.

Secondly, Applicant has failed to provide a convincing argument with respect to the enablement of the present invention. As discussed *supra*, the effect of arsenic on the human body is unpredictable and in fact is in most cases undesirable. Further, it is clear that the data sets used by the Applicant to arrive at the instant invention are subject to interpretation. In fact, only the Applicant's work supports the interpretation that has been used to arrive at the instant invention. All other prior art arrive at the opposite conclusion (*i.e.* arsenic is harmful at the levels instantly claimed). As such, it is clear that to practice the claimed invention will require undue experimentation, with no assurance of success. At the very least, the skilled artisan would be required to determine: 1) a form of arsenic suitable for inclusion in drinking water; 2) a method of incorporating (or lowering), maintaining and monitoring the level the of arsenic in drinking water; and 3) a method of monitoring the population of people ingesting the drinking water. Applicant has provided no specific guidance or direction with respect to the instantly claimed methods.

Thirdly, Applicant has argued that no patent claim is made that arsenic should be lowered to around 50 μg/L from higher levels. This is not true. The claims are directed to methods for reducing cancer morbidity and mortality in men and women by "**adjusting** the arsenic level in drinking water to 25-<75 μg/L". Clearly, "adjusting" means raising or lowering. If the arsenic level is above 75 μg/L, adjusting to 25-<75 μg/L would require that the level of arsenic be lowered. Applicant has again provided no guidance or direction on any methods of lowering the level of arsenic in drinking water.

Lastly, although Applicant is correct that the current EPA standards do not diminish the inherent "value or worth" of the instant invention, they do in fact support the lack of enablement of the claimed invention. It is clear that scientists and regulators recognize the inherent toxicity of arsenic in drinking water. This is supported by the fact that the EPA lowered the acceptable levels of arsenic in drinking water to levels lower than those instantly claimed.

Conclusion

No claims are allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR § 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR § 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR § 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR § 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James D. Anderson whose telephone number is 571-272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Patent Examiner
AU 1614

January 16, 2007

PHYLLIS SPIVACK
PRIMARY EXAMINER